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Role of Mathematical Concepts in Cancer Research

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The role of mathematics in cancer research is not confined to epidemiology (population level). The expected contribution of it in various levels is exemplified stepwise. At the individual level, prediction of life expectancy of a cancer case or psychological analysis of life-threatened patient; at the tissue level, stochastic estimation of future metastases; at the cellular level, model construction for abnormal metabolic processes in malignant cell; at the molecular level, elucidation of carcinogenetic mechanism from a thermodynamic standpoint of view.

Throughout this conference, the role of mathematical concepts in cancer research was fully substantiated in the framework of epidemiology. However, they are naturally not confined to this field (population level), but also expected to function in other areas such as individual, tissue, cellular, and molecular levels of cancer research.

Individual Level

With the increased accumulation of empirical data, the life expectancy curve for cases of cancer in various sites is drawn more definitely, and even the outcome of each individual patient is forecast more precisely with the increase of clinical and epidemiological knowledge.

It is already established that such factors as site, size, or histopathological attributes of the cancer, age, sex, and hereditary disposition of the host, and medical and surgical intervention are the important variables in the survival function of cancer patients, and the implication of each factor decided their fate is being elucidated more definitely. In accordance with this advance, the risk factors acting in deterioration of the clinical course will be elucidated and valuable information for the rehabilitation of the patient will be also provided.

But, for the sake of the patient, the precise prediction of his own fate is sometimes not only needless, but also unfavorable to his state of mind. It is, therefore, recommended that the statistical methodology be applied for the benefits of the patients such as the analysis of unusual factors and to alleviate under the challenging stress imposed by knowledge of his malignancy. His phenotypic psychological response should be highly variable, depending on his personality, individual circumstances and cultural background, but whatever response he might show, he is surely looking for the psychological aid besides the medicosurgical techniques, and the former can be analysis in cooperation with the sympathetic clinical psychologists.

Tissue Level

The prediction of the possible site of metastasis is valuable in clinical practice, because it makes postoperative control of cancer patients more effective. Cancer cells are transferred from primary focal lesion to other tissues or organs through hematogenous and lymphogenous pathways. The probability of such a metastatic process is determined by the anatomical configuration of blood and lymphatic vessels as well as the histotopographical characteristics of the primary cancer.

The flow and settlement of cancer cells are purely stochastic phenomena, and, therefore, prediction will be feasible, provided the initial condition and probability distribution of various factors are identified. Here, also, the active commitment of the statisticians is expected along with that of the pathologists.

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Cellular Level

It is generally admitted that cancer cells differ from normal cells in an accelerated growth rate which is presumably caused by some disturbances in feedback mechanism. But the intricately interrelated structure of many metabolic pathways in a cell is too complicated to be elucidated by biochemical approach, and, therefore, mathematic concepts are not applicable to such a system, unless it is identified in biochemical terms.

Yet the dynamics of the complicated flow of chemical reactions involving substrates and enzymes is in principle dominated ubiquitously by the chemical rate constants in each reaction step, and an appropriate model simulating the most substantial part of such a stochastic feedback system can provide us with insight into the differences in chemical dynamics between normal and cancer cells.

Regarding this problem, Masuyama (*1*) states that some stochastic rule dominates the distribution of such biochemical characteristics as metabolite, enzyme, hormone, or toxic substance concentrations in the body, and even the excretion rate constants among the organisms.

Molecular Level

It might be reasonably anticipated that the first step in the carcinogenic process in an organism is a tiny modification in a molecule of nucleic acid. However minute it might be, it is an initiation of the carcinogenic process which could proceed indefinitely until the host organism cannot bear it any more. From thermodynamic standpoint of view, such a change might be explicable as a state transition from normal to malignant in a relevant molecule, accompanying the increase of entropy terms.

If it is further presumed that there is an energy barrier between these two imaginary molecular states, the frequency of transition is expected to correspond to the probability of crossing over the barrier, and this is expressed by Boltzmann's distribution in terms of activation energy and absolute temperature.

It is very interesting here to recall the work of Pullman and Pullman (*2*), in which they showed that polycyclic hydrocarbons are carcinogenic as far as their absorption spectrum is within some definite range of wavelength. According to quantum mechanics, the tunnel effect is another way to accomplish the break-through over the energy barrier. If intermolecular resonance had something to do with this effect, the story would become more stimulating to our imagination. We place our hopes in quantum mechanics for the elucidation of the carcinogenic process in molecular terms.

Conclusion

In conclusion, mathematical approaches usually intend to develop their concept quantitatively, but medical approaches always emphasize the qualitative nature of their objectives. What is essentially needed, I think, is not reconciliation between them, but a dialectic synthesis in Hegel's sense.

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